REMARKS

Pursuant to 37 C.F.R. § 1.116, Applicants submit that the amendments presented herein are made to i) cancel claims or comply with any requirement of form expressly set forth in a previous Office action, or ii) present rejected claims in better form for consideration on appeal.

With the present amendments, Applicants have canceled the claims directed to the vaccine compositions and amended claims 46-48 directed to immunizing cattle by incorporating the substance of claims 1, 2 and 40, on which they depend. Claims 46-48 are further amended by reciting that the method is a method of immunizing cattle without significant injection site lesion formation and that the encapsulating polymer adjuvant releases antigens slowly at the site of injection without significant, permanent injection site lesion formation.

Example 8, beginning on page 52 of the specification supports the limitation that the method avoids significant injection site lesion formation, both numbers and size of lesions are reduced. The data supporting these results are also found in tables 12, 13 and 14 accompanying example 8.

Support for the definition of the polymer as being an encapsulating polymer is found in the specification, for example, on page 15, lines 23-27, on page 21, lines 1-10, and on page 21, lines 27 thru page 22, line 2.

In the Office Action of October 5, 2006, the Examiner rejected claims 1-3, 15, 17-19 and 40

under 35 U.S.C. § 102(a) for being anticipated by Roberts (WO 94/22476). The Examiner concluded that Roberts teaches a multicomponent clostridial vaccine containing an antigen from *M. bovis* and/or *H .somnus* and a polymer adjuvant, wherein the dose is 3 ml or less. The Examiner further states, "Here, Roberts, may be relied upon because it reasonably suggest[s] to one having ordinary skill in the art the administration of multicomponent vaccines in low dose volumes of about 3 ml or less having dispersible, soluable adjuvants. Roberts states that potent adjuvants such as carbopol have been used in clostridial vaccines. Therefore, Roberts have disclosed the polymer adjuvant even though Roberts may refer to polymer adjuvants as nonpreferred embodiments. Polymer adjuvants, including carbopol, are known to readily absorb water and due to its hydrophilic nature, and cross-linked structure, are known to [be] useable for controlled release drug delivery systems. Carbopols were first prepared in 1957 and since then many extended release formulations have been presented in the art. Therefore, Roberts teaching of a dispersible, soluble adjuvant, encompasses polymer adjuvants, just as required by the claims."

It is respectfully submitted that dispersible, soluble adjuvants are not polymer adjuvants. Polymer adjuvants are referred to as "depot" adjuvants by Roberts. The Examiner is putting together two opposing teachings of Roberts.

On page 1, the first full paragraph, Roberts states:

> "The present invention relates generally to vaccine compositions and methods of using the same. More specifically, the invention pertains to multicomponent clostridial vaccines made without stabilizing carriers or depot adjuvants, but rather with a readily dispersible, water-soluble adjuvant, saponin."

On page 2, the paragraph beginning on line one, Roberts recites:

> "Other potent depot adjuvants, such as water-in-oil emulsions and carbopol, have also been used in clostridial vaccines. The above-described adjuvants, although increasing antigenicity, usually provoke severe persistent local reactions, such as granulomas, abscesses and scarring, when injected subcutaneously or intramuscularly. These local reactions are, in turn, responsible for carcass blemish which requires expensive trimming, a consideration when the vaccine has been injected into muscle tissue destined to be a valuable cut of meat."

On page 2, in the paragraph beginning on line 22, Roberts recites:

> "The present invention is based on the surprising discovery that the water-soluable adjuvant, saponin, can be used in place of a depot adjuvant in multicomponent clostridial vaccines for cattle."

On page 4, in the paragraph beginning on line 24, Roberts states:

> "Central to the present invention is the surprising discovery that stable, potent, multicomponent clostridial vaccines can be made without the use of depot adjuvants. In particular, the present invention provides for vaccines including rapidly dispersed, soluble adjuvants, that is, adjuvants that are not retained at the injection site for a significant period of time, thereby exhibiting low tissue reactivity. The vaccines can be administered intramuscularly and subcutaneously without the harmful side effects and chronic inflammatory responses that produce granulomas and abscesses, seen with other clostridial vaccine compositions when administered via these routes."

On page 6, in the paragraph beginning on line 13, Roberts teaches:

> "The above-described bacterins and toxoids are administered in vaccine compositions including a readily dispersible (*i.e.*, non-depot), soluble adjuvant, thereby avoiding chronic irritation at the injection site. Such adjuvants include, for example, mild oil-in-water emulsions made with mineral oil, such as, for example, Amphigen (U.S. Patent No. 5,084,269) and cytokines, such as any of the various interleukins or interferons."
>
> "Particularly preferred dispersible, non-depot adjuvants for use with the present vaccine compositions are saponins."

In view of this disclosure of Roberts, it is incorrect to state that "Roberts have disclosed the Polymer adjuvant even though Roberts may refer to polymer adjuvants as nonpreferred embodiments." Roberts is teaching against using polymer adjuvants, which are depot adjuvants, at any dosage. As quoted above, Roberts states, "[i]n particular, the present invention provides for vaccines including rapidly dispersed, soluble adjuvants, that is, adjuvants that are not retained at the injection site for a significant period of time, thereby exhibiting low tissue reactivity."

It can not be concluded that "Roberts teaching of a dispersible, soluble adjuvant, encompasses polymer adjuvants, just as required by the claims." Roberts' dispersible adjuvants are not polymer adjuvants. Roberts further fails to anticipate the present invention as the dose size taught by Roberts is for vaccine compositions according to the Roberts invention. Not vaccines containing polymers. On page 8, beginning line 30, Roberts states:

> "For example, to immunize cattle with the clostridial vaccine compositions described above [Roberts' compositions with non-depot adjuvants], generally between 0.5 ml to 10 ml will be administered, more preferably 1 to 5 ml."

Roberts teaches nothing about the dosages of the prior art polymer adjuvanted vaccine

compositions.

Applicants' invention is the discovery that low dose multicomponent clostridial vaccines can provide protection when used with encapsulating (depot) polymer adjuvants if they are administered in low doses, as the polymer causes the release of the antigen to occur over an extended period of time, while the low dose avoids the formation of significant injection site lesions that remain present. This is not suggested by Roberts.

Roberts solved the problem of injection site lesions using a dispersible adjuvant. Applicants solve the same problem using low dose compositions with an encapsulating (depot) adjuvant. There is no prior art that teaches the use of multicomponent clostridial vaccines with encapsulating polymer adjuvants administered in low doses of 3 ml or less.

The Examiner has stated that a reference may be relied on for all that it would have reasonably suggested to one having ordinary skill in the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d804 (Fed. Cir.)(1989). The depot polymer disclosure was taught by Roberts to contrast the Roberts dispersible adjuvant invention, it is not an embodiment of the Roberts invention at all, not even a nonpreferred embodiment. The dose sizes taught by Roberts are for vaccines containing dispersible adjuvants, not depot adjuvants. Roberts reasonably suggests not using polymer adjuvants.

Applicants' invention is the discovery that encapsulating polymer adjuvants can be used at very low doses of vaccine without significant injection site lesion formation. This is not suggested by Roberts, as Roberts teaches against using any vaccine compositions with depot adjuvants at any dose size because of injection site lesion formation. Nor does this prior art teach the effectiveness of low dose polymer adjuvanated multicomponent clostridial vaccines. What

this reference reasonably suggests to one having ordinary skill in the art is to avoid depot type polymer adjuvants. The Examiner attempts to put together the contrasting prior art against which Roberts compares his vaccine together with the invention disclosed by Roberts. The Examiner is correct that Roberts may be relied on for suggesting to one of ordinary skill "the administration of multicomponent vaccines in low dose volumes of about 3 ml or less having dispersible, soluble adjuvants". The conclusion is incorrect, however, that Roberts disclosed using a polymer adjuvant in such vaccine compositions at low doses. Roberts does not refer to such compositions as nonpreferred embodiments. This is the prior art that presents the problem of injection site lesions, which Roberts solves using dispersible adjuvants.

For the reasons set forth above, the Examiner's rejection of claims 46-48 under 35 U.S.C. § 102(a) for being anticipated is also incorrect and should be withdrawn. In summary, the Examiner has combined Roberts' teaching with what Roberts is teaching against, asserting incorrectly that what Roberts is teaching against is an embodiment, even if not a preferred one. No where in Roberts can one find the suggestion of using a low dose of multicomponent clostridial vaccine comprising a polymer adjuvant or that any vaccine comprising a polymer adjuvant could be used without significant injection site lesion formation.

Claims 46-48 have being objected to under 37 CFR 1.75(c) for being of improper dependent form.

Applicants respectfully submit that it would be perfectly possible to immunize a bovine animal with a cattle vaccine. However, with the amendments to claims 46-48, the reference to a bovine animal has been replaced with cattle in order to advance the prosecution of this application.

Claims 46-48 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite for being drawn to a method immunizing a bovine animal. As noted above, the present amendments to those claims have overcome this basis for objection.

In view of the above it is respectfully submitted that claims 46-48, all claims now in the application, are in condition for allowance. Favorable action is solicited.

Should the Examiner consider a conference would be helpful in advancing the prosecution of this application, she is invited to telephone Applicants' attorney at the number below.

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Respectfully submitted,

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Enclosure: Notice of Appeal (2 pages)